CAT

FACSIMILE MESSAGE

To: SEAN WALTON

Fax No:

From: JOHN Mc CAFFERTY

Date:

No. of pages inc cover sheet: 3

SEAN,

I ENCLOSE A COPY OF A PAGE FROM GEORGE SMITH, IN THE INTRO. FOR A BOOK I AM CO-EDITING. I AM VERY UNCOMFORTABLE WITH THE UNDERLINED SECTION. I HAVE TRIED TO DIFFUSE IT AS YOU WILL SEE FROM THE ACCOMPANYING E. MAIL MESSAGE. WHAT IS YOUR ADVICE. SHOULD I PULL OUT AS EDITOR IF IT IS NOT CHANGED?

JJ Mc Cafferty

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antibodies. I was inspired by a new vision. I imagined a universal library of single-chain antibodies displayed on phage. The antibodies would have one or a few framework sequences, but their CDRs (complementarity-determining regions) would be randomized to generate a vast diversity of binding specificities. The user could use any antigen of interest to affinity-purify clones whose displayed antibodies happened to bind that antigen. In this way, monoclonal antibodies might be obtained to almost any antigen by simple microbiological means, without the need for animals or animal cells in culture. I thought these artificial antibodies would eventually replace conventional and monoclonal antibodies for many purposes. The new idea, which I dubbed "infectious antibodies" (now called phage antibodies), became a key aspect of the new grant proposal I submitted to NIH on November 1, 1988.

The eventful year of 1988 closed appropriately with yet another broadening of my horizons. On December 15, I was sitting in Jim Larrick's office at Genelabs, Inc. "Drugs!" he said cryptically. He explained that if the epitope library were used to find new peptide ligands for receptors other than antibodies, these ligands would represent a new and broadly applicable route to drug candidates. It was so obvious! Yet, up to then my plans had been exclusively immunological—reflecting, I suppose, my doctoral and postdoctoral training in that field. From that day on, drug discovery was to become a new element in my concept of phage-display technology.

Work on the epitope library did not begin in earnest until the summer of 1989, both because I was occupied with other projects and because my lab was not funded between May 1988 and July 1989, when my new NIH grant—finally successful!—started. Two people came to the lab then; Jamie Scott, a postdoctorate student who constructed and tested our first epitope library, and has been my close collaborator ever since; and a new technician, Robert Davis, who carried out many of the key experiments and has managed my lab now for six years.

When I look back on my year of discovery, I'm struck—and a little embarrassed—at how parochial my vision of phage display was at the beginning, before my education at the hands of my fellow scientists. Phage-display technology, as we now understand it, and as is exemplified in this book, has been very much a communal invention. There's little sense in trying to apportion credit for such advances to individuals—for patent purposes or any other reason. But there is much sense, I think, in maintaining a vigorous, public community of scientists, talking freely with one another, whose ideas, excitement, and results are selected, amplified, recombined, tested, and reselected much as are the phage libraries.

George P. Smith
Division of Biological Sciences
University of Missouri

To: Brian-Kay
From: cat@cityscape.co.uk (John McCafferty)
Subject: Smith Preface

Dear Brian,

On 29th of this month I sent the following message and have not had a reply from you.

"In the preface (pg xix line 9-11) George Smith makes a comment about "infectious antibodies" and refers to a grant proposal he made on these. Since he is not known in the field for his work with antibody display perhaps you could get him to add/dictate a line to say what happened to his attempts to display antibodies. Otherwise it is rather open ended".

I must stress that I think he should say more or he should say less.While he dismisses the importance of patents at the end of his contribution, it is an important aspect of work within companies such as our own. Unlike Smith and Ladner I did not use this book as a forum for presenting the CAT patent case. This type of statement makes my own association as editor of the book very difficult. I would appreciate your earliest action and reply on this.

Regards,

John

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